IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Silvio Aime	Confirmation No. 9446
Serial No.:	10/552,851	
Filing Date:	March 19th, 2010.	
Examiner:	Rider Lance	
Group Art:	1618	
For:	ADDUCTS BETWEEN MAGNETIC RESONANCE SHIFT REAGENTS AND SUBSTRATES CONTAINING EXCHANGEABLE PROTONS FOR CEST APPLICATIONS	

Mail Stop **Amendment**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

RESPONSE TO NON-FINAL OFFICE ACTION

In response to the non-final Office Action mailed on March 19, 2010, Applicants respectfully request entry and consideration of this Response. This response is timely filed by June 21st, 2010 provided that June 19th was a Saturday. 10, 2009.

Amendments to the Claims begin on page 2 of this paper

Remarks begin on page 8 of this paper.

Amendments to the Claims

1-9 (Cancelled)

10. (Currently Amended) A method of imaging a subject comprising the steps of administering into a subject a paramagnetic CEST agent comprising a substrate molecule (SH) endowed with at least one mobile proton in exchange with bulk water bound by means of electrostatic interactions to a paramagnetic chelate complex (SR) of a metal ion selected from iron (II) (high-spin configuration), iron (III), cobalt (II), rhodium (II), copper (II), nickel (II), cerium (III), praseodymium (III), neodymium (III), dysprosium (III), erbium (III), terbium (III), holmium (III), thulium (III), ytterbium (III) and europium (III); and imaging said subject using a CEST based MRI procedure.

11. (Previously Presented) The method of claim 10 wherein the substrate molecule (SH) is diamagnetic and is selected from linear and cyclic polyamines, polyaminoacids, proteins, polysaccharides, polyamidoamine, peramidated polyaminoacids, dendrimers containing amide groups, polycyclodextrins, polysaccharides and alginates.

12. (Previously Presented) The method of claim 11 wherein the substrate is selected from polyarginine, albumin and cyclen.

13. (Previously Presented) The method of claims 10 in which the paramagnetic chelate is $[LnDOTP]^{4-}$ and the Ln metal ion is selected from the following: Ce(III), Pr(III), Nd(III), Eu(III), Tb(III), Dy(III), Ho(III), Er(III), Tm(III), Yb(III).

14. (Previously Presented) The method of claims 10 wherein the substrate molecule (SH) and the paramagnetic chelate complex (SR) are compartimentalized in

biocompatible systems selected from the group consisting of liposomes, nanoparticles, microemulsions and protein cavities.

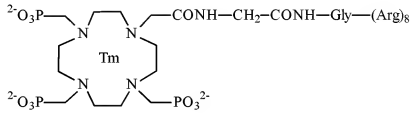
15. (Cancelled) .

16. (Currently Amended) The method of claim 10 wherein the electrostatic interaction between the substrate molecule (SH) and the paramagnetic chelate complex (SR) are bound by means of electrostatic interactions having a thermodynamic constant of association Ka greater than 10.

17. (Cancelled)

18. (Withdrawn) A paramagnetic CEST agent comprising a substrate molecule (SH) endowed with at least one mobile proton in exchange with bulk water bound to a $[LnDOTP]^{4-}$ as paramagnetic chelate complex (SR).

19. (Withdrawn) A paramagnetic CEST agent of formula:



20-21 (Cancelled).

22. (Withdrawn) The paramagnetic CEST agent of claim 18 wherein the substrate molecule SH is bound to the chelate complex by means of electrostatic interactions having a thermodynamic constant of association Ka greater than 10.

23. (Withdrawn) The paramagnetic CEST agent of claim 18 wherein the substrate molecule (SH) is selected from linear and cyclic polyamines, polyaminoacids, proteins, polysaccharides, polyamidoamine, permidated polyaminoacids, dendrimers containing amide groups, polycyclodextrins, polysaccharides and alginates.

24. (Withdrawn) A paramagnetic CEST agent comprising a paramagnetic chelate complex (SR) of a metal ion selected from iron (II) (high-spin configuration), iron (III), cobalt (II), rhodium (II), copper (II), nickel (II), cerium (III), praseodymium (III), neodymium (III), dysprosium (III), erbium (III), terbium (III), holmium (III), thulium (III), ytterbium (III) and europium (III), bound to a substrate molecule (SH) endowed with at least one mobile proton, wherein the said SR and SH are compartmentalized in a biocompatible system selected from liposomes, nanoparticles, microemulsions and protein cavities.

25. (Withdrawn) The paramagnetic CEST agent of claim 18 or 24 wherein the exchangeable protons belong to water molecules.

26. (Withdrawn) A paramagnetic CEST agent comprising a paramagnetic chelate complex (SR) and water molecules, whose chemical shift is influenced by the SR unit, trapped in the same compartment and wherein, at the same time, the said water molecule are in exchange conditions with the bulk water.

27. (Withdrawn) A diagnostic composition comprising the agent of any one of claims 18, 19, 24, 25 or 26 together with a suitable vehicle.

28. (Cancelled)